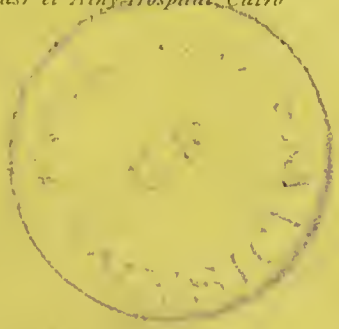
Research Defence Society

SLEEPING SICKNESS

BY

F. M. SANDWITH, M.D.

Fellow of the Royal College of Physicians, London: Gresham Professor of Physic; Lecturer at the London School of Tropical Medicine and at St. Thomas's Hospital Medical School; Senior Physician to the Albert Dock Hospital; and Consulting Physician to Kasr el Ainy Hospital, Cairo



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PREFACE

EVERYONE must agree with the Secretary of State for the Colonies, who told the House of Commons on June 27th, 1912, that undoubtedly the most anxious problem of the present and the future in connection with tropical medicine, is that of sleeping sickness.

Yet, in spite of the voluminous literature which has appeared on the subject during this century, there is no popular history of the disease in the British tongue, though the Germans are indebted for a very good one to that master of science, the late Professor Koch. The Director of the Tropical Diseases Bureau, whom I have to thank for many favours, has therefore encouraged me to write these pages, which were, in the first instance, delivered as three lectures at Gresham College, in February last, appeared in print in the *Medical Press and Circular* in April, and are now published by the combined desire of the Research Defence Society and of the Gresham Committee, which has kindly contributed a grant towards their publication.

I shall be rewarded if this brief account of other men's labours proves to be of any value to a few of the many English-reading explorers, missionaries and merchants in Africa, who are living within the danger zone, and, last but not least, to their many relatives and friends in this country.

31 CAVENDISH SQUARE, LONDON,
October, 1912.

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SLEEPING SICKNESS

Cattle Trypanosomiasis.

It is a well-known fact that, when Great Britain acquired her first colonies, the bold spirits who embarked on distant adventure were actuated, partly by a fine spirit of enterprise, but greatly also by the desire of gain, and for many years the mother country looked upon her colonies merely as a source of plunder.[1] But as time went on she learnt some bitter lessons, and terrible upheavals, such as the secession of the great American Colonies and the Indian Mutiny, caused it to be borne in upon her that possession also meant responsibility. Wherever British influence is now recognised we have learnt to take upon us the white man's burden, to find out the scourges of the country we profess to protect, and to endeavour to rid it of its enemies. In this the United States of America, France and Germany are not behindhand, but in proportion as our Colonies are larger than those of other countries, so much greater is the work to be done by Englishmen, and I think we may say that we have not been faithless to our task.

Since the days of early travellers in Africa, a scourge of the greatest magnitude to natives and to Europeans has been that of the tsetse fly (*Glossina morsitans*). Until lately it was not known why the bite of this insect caused cattle, horses, and many other domestic animals to die of a definite disease, but the fact that this occurred was known to all, and many native remedies were employed, all more or less useless.

[1] Sheridan described the East India Company as "highwaymen in kid gloves."

For instance, that great medical missionary and explorer, David Livingstone, found in his travels that some tribes in Africa believed that lion's fat, smeared on the tail of an ox, would prevent the bite of the insect, and for this purpose lion's fat was conveyed from districts where the king of beasts was plentiful. Again, he came across a remedy consisting of the bark of a root unknown to him, which was mixed with a dozen dried tsetse flies, ground together into a fine powder, and then administered internally to the animals whenever symptoms appeared; the cattle were also fumigated by burning under them the rest of the plant pertaining to the root. The chief who told him of this secret and somewhat homœopathic remedy frankly admitted that it would not cure all the bitten cattle.

In Livingstone's writings we find the tsetse fly and its ravages referred to again and again. Thus, in his "Missionary Travels," published in 1857, he writes :—

"On approaching the confluence of the Tamunak'le we were informed that the fly called 'tsetse' abounded on its banks. This was a barrier we never expected to meet; and as it might have brought our waggons to a complete standstill in a wilderness, where no supplies for the children could be obtained, we were reluctantly compelled to recross the Zouga." Then this keen observer goes on to tell us of the fly, and by our modern knowledge we can see how near to the truth both the native traditions and his own deductions arrived.

"The cattle, in rushing along the water in the Mababe, probably crossed a small patch of trees containing tsetse, an insect which was shortly to become a perfect pest to us." "We had come through another tsetse district by night, and at once passed our cattle over to the northern bank to preserve them from its ravages.

"A few remarks on the tsetse, or *Glossina morsitans*, may here be appropriate. It is not much larger than the common house-fly, and is nearly of the same brown colour as the common honey-bee; the after part of the body has three or four yellow bars across it, the wings project beyond this part considerably, and it is remarkably alert, avoiding most dexterously all attempts to capture it with the hand, at common temperatures; in the cool of the morning and

evening it is less agile. Its peculiar buzz, when once heard, can never be forgotten by the traveller whose means of locomotion are domestic animals, for it is well known that the bite of this poisonous insect is certain death to the ox, horse and dog. In this journey, though we were not aware of any great number having at any time lighted on our cattle, we lost forty-three fine oxen by its bite. We watched the animals carefully, and believe that not a score of flies were ever upon them.

"A most remarkable feature in the bite of the tsetse is its perfect harmlessness to man and wild animals, and even calves so long as they continue to suck the cows. We never experienced the slightest injury from them ourselves, personally, although we lived two months in their habitat, which was in this case as sharply defined as in many others, for the south bank of the Chobe was infested by them, and the northern bank, where our cattle were placed only fifty yards distant, contained not a single specimen. This was the more remarkable, as we often saw natives carrying over raw meat to the opposite bank with many tsetse settled upon it.

"The poison does not seem to be injected by a sting, or by ova placed beneath the skin, for, when one is allowed to feed freely on the hand, it is seen to insert the middle prong of three portions into which the proboscis divides, somewhat deeply into the true skin; it then draws it out a little way, and it assumes a crimson colour as the mandibles come into brisk operation. The previously shrunken belly swells out, and, if left undisturbed, the fly quietly departs when it is full. A slight itching irritation follows, but not more than in the bite of a mosquito. In the ox this same bite produces no more immediate effects than in a man. It does not startle him as the gad-fly does; but in a few days afterwards the following symptoms supervene: the eyes and nose begin to run, the coat stares as if the animal were cold, a swelling appears under the jaw, and sometimes at the navel; and, though the animal continues to graze, emaciation commences, accompanied with a peculiar flaccidity of the muscles, and this proceeds unchecked until, perhaps months afterwards, purging comes on, and the animal, no longer able to graze, perishes in a state of

extreme exhaustion. Those which are in good condition often perish soon after the bite is inflicted with staggering and blindness, as if the brain were affected by it. Sudden changes of temperature produced by falls of rain seem to hasten the progress of the complaint; but in general the emaciation goes on uninterruptedly for months, and, do what we will, the poor animals perish miserably.

"When opened, the cellular tissue on the surface of the body beneath the skin is seen to be injected with air, as if a quantity of soap bubbles were scattered over it, or a dishonest, awkward butcher had been trying to make it look fat. The fat is of a greenish-yellow colour, and of an oily consistence. All the muscles are flabby, and the heart often so soft that the fingers may be made to meet through it. The lungs and liver partake of the disease. The stomach and bowels are pale and empty, and the gall-bladder is distended with bile.

"These symptoms seem to indicate what is probably the case—a poison in the blood, the germ of which enters when the proboscis is inserted to draw blood. The poison germ, contained in a bulb at the root of the proboscis, seems capable, although very minute in quantity, of reproducing itself, for the blood after death by tsetse is very small in quantity, and scarcely stains the hands in dissections.

"Many large tribes on the Zambesi can keep no domestic animals, except the goat, in consequence of the scourge existing in their country. Our children were frequently bitten, yet suffered no harm; and we saw around us numbers of zebras, buffaloes, pigs, pallahs and other antelopes feeding quietly in the very habitat of the tsetse, yet as undisturbed by its bite as oxen are when they first receive the fatal poison. There is not so much difference in the natures of the horse and zebra, the buffalo and ox, the sheep and antelope, as to afford any satisfactory explanation of the phenomenon. Is a man not as much a domestic animal as a dog? The curious feature in the case, that dogs perish though fed on milk, whereas calves escape so long as they continue sucking, made us imagine that the mischief might be produced by some plant in the locality, and not by the tsetse; but Major Vardon, of the Madras Army, settled that

point by riding a horse up to a small hill infested by the insect, without allowing him time to graze, and, though he only remained long enough to take a view of the country and catch some specimens of tsetse on the animal, in ten days afterwards the horse was dead.

"There is no cure yet known for the disease. A careless herdsman allowing a large number of cattle to wander into a tsetse district loses all except the calves; and Sebutuane once lost nearly the entire cattle of his tribe—very many thousands—by unwittingly coming under its influence. Inoculation does not insure immunity, as animals which have been slightly bitten in one year may perish by a greater number of bites in the next; but it is probable that with the increase of guns the game will perish, as has happened in the south, and the tsetse, deprived of food, may become extinct simultaneously with the larger animals."

In 1895 the Honourable Sir Walter Hely-Hutchinson, then Governor of Natal and Zululand, persuaded Surgeon-Major (now Sir David) Bruce, of the Army Medical Service, to investigate and report upon the disease as it occurs in Zululand. Accompanied by his competent wife as his sole laboratory assistant, Major Bruce proceeded to that part of the country where tsetse were abundant, and carried out minute and patient investigations. He found that the disease affected almost all the domestic animals, that its duration varied from a few days or weeks to many months, that it is invariably fatal in the horse, donkey or dog, but that a few cattle recover. The local name, "Nagana," means in the Zulu language to be "depressed" or "low spirited," but the name varies in different countries, and the disease is often known simply as the "fly disease," from the correct assumption that it is caused by the bite of the tsetse fly.

By many experiments on animals and by microscopical examinations, Major Bruce proved that the tsetse fly (*Glossina morsitans*) was indeed the cause of the disease, and he proved likewise that it did not, as had been popularly supposed, inject into the bitten animal a poison elaborated by itself, but that the tsetse acts as the carrier "of a living virus, an infinitely small parasite, from one animal to another, which, entering into the blood stream of the animal

bitten or pricked, there propagates and so gives rise to the disease."

The parasites conveyed by the flies, and found by Major Bruce to be present in the blood of every affected animal, are trypanosomes (*Trypanosoma brucei*), which can be seen under a powerful microscope as transparent, elongated bodies, pointed or somewhat blunt at one end, with a fine lash at the other, which is in constant whip-like motion. They can be seen quite distinctly, wriggling among the red blood corpuscles and causing much commotion. It was not known how the parasite caused the death of its host, but it was thought probable that it did so by the production or secretion of some poisonous substance.

The tsetse flies which are the carriers of these parasites haunt certain very definitely prescribed areas, and, on entering these regions, the unfortunate travellers and animals are instantly attacked. "On entering the fly country," writes Major Bruce, "one is not left long in ignorance of the presence of the tsetse. The natives may be seen slapping their naked legs, the dogs bite round, and the horses kick." Unlike the mosquito, both sexes of the fly bite alike.

It was evident to Major Bruce that the fly procured the parasite which caused the disease from some definite source, and European hunters and natives stated that wild game—buffalo, wildebeeste, water buck and koodoo—must be present where the disease was found. Where there was no game, they maintained, there was no *nagana*. Major Bruce therefore microscopically examined the blood of various species of wild game to see if he could find in it the minute trypanosomes which give rise to the disease. But the parasites are not sufficiently frequent in the blood to be detected. He then injected the blood of such game, immediately after death, into healthy dogs, and some of these animals, though not in a fly country, subsequently showed the characteristic symptoms of *nagana*. He thus proved that several species of wild beasts, living in a fly country, harbour the *nagana* parasites, apparently without producing in them any great discomfort, though they may occasionally suffer from its effects and even die in consequence.

The tsetse fly, carrying the infected blood of the wild

game, and injecting it by its proboscis into healthy domestic animals, cause the latter to develop *nagana*, for the parasite is to them infinitely more deadly than it is to wild game. When such an animal is examined after death the body is seen to be extremely emaciated, but *nagana* is a disease in which the organs show very few alterations.

In horses, donkeys and cattle which have died of *nagana*, the spleen and liver are enlarged, there are masses of yellow, jelly-like material under the skin and mucous membranes, also between the muscles, and patches of extravasation of blood are found under the pericardium.

Immediately after death, the trypanosomes in the animal lose their vitality, so that in twenty-four hours there are usually no longer any active parasites in the blood or in the internal organs.

The fly lives on animal blood and on that alone, and therefore haunts those districts inhabited by game; it was formerly thought capable of infecting a healthy animal forty-eight hours after absorbing the blood of one affected with *nagana*, but after three days it seemed to have lost its infectivity. We know that the fly and the game both require shade and water, therefore it is not surprising that they are both found in the same localities.

So far Major Bruce's investigations proved successful. He banished all the obscurity surrounding the disease by proving beyond any doubt that it was caused by the trypanosomes he had found in the blood of the affected animals, and not in healthy ones, and that this trypanosome was conveyed by this particular tsetse fly, either from wild game, in which the trypanosome occurs as a comparatively harmless parasite, to domestic animals, to which it is deadly, or from sick animals to healthy animals. But the practical object of these investigations has not yet been attained. We have not yet found either a preventive or a cure. Either we must aim at the destruction of the cause, or we must seek to render domestic animals immune, even as the wild game appears to be immune, or, lastly, we must discover some drug or serum which will cure the disease. Of drugs, arsenical preparations have proved to be more successful than others, but they are not uniformly, or even often, of any permanent value.

I have given this brief account of Sir David Bruce's investigations into *nagana* for two reasons; because (1) it is a disease of immense importance to the opening out and colonisation of Africa; it is a scourge which forbids farming in large districts of Africa, and makes all movements of cattle, horses, and other domestic animals so grave a risk that travelling, except on foot, is well nigh impossible, except, of course, where railways have been laid down; (2) the illness has gained in importance to us because recent investigations have proved it to be a parallel disease to the one I am now about to describe—the sleeping sickness of tropical Africa, which is a human trypanosomiasis, in many ways similar to the trypanosomiasis, or *nagana*, of animals.

History of Sleeping Sickness.

Sleeping sickness has acquired its name from one of the most prominent symptoms of the last stage of the disease. It is an infectious illness, generally of a chronic nature, though occasionally it assumes an acute form, attacking chiefly the central nervous system. It is caused by the action of trypanosomes which are found in the blood, the lymphatic glands, and eventually in the cerebro-spinal fluid of the patient, and which have been conveyed to the patient by the bite of a tsetse fly, the *Glossina palpalis*. It is a disease the distribution of which is undoubtedly gaining in magnitude, and for which, up to the present date, there has been found no certain cure.

The earliest mention of the disease is in a book by John Atkins, a Naval Surgeon, who wrote of the "physical observations on the coast of Guiney." This book was printed "at the Looking Glass, over against St. Magnus' Church, London Bridge," in the year 1742. He wrote:—

"The sleeping distemper (common among negroes) gives no other previous notice than a want of appetite two or three days before; their sleeps are sound and sense of feeling very little, for pulling, drubbing, or whipping will scarce stir up sense and power enough to move, and the moment you cease beating the smart is forgot, and down they fall again into a state of insensibility, drivelling constantly from the mouth, as if in a deep salivation; breathe slowly, but not unequally, nor snort.

"Young people are more subject to it than the old; and the judgement generally pronounced is death, the prognostick seldom failing. If now and then one of them recovers, he certainly loses the little reason he had and turns idiot."

This very unsympathetic account is sufficiently clear to make us sure that the disease was no other than the sleeping sickness with which we are now, unfortunately, much more familiar.

The next authority is Dr. Winterbottom, a Colonial Surgeon, who published, in 1803, an account of the disease as he saw it along the Bight of Benin, on the West Coast of Africa. "The Africans," he writes, "are very subject to a species of lethargy which they are much afraid of, as it proves fatal in every instance." He and all later observers until recent times diagnosed the disease from the characteristic symptoms of the later stages—the somnolence and muscular weakness. But he mentions that "small glandular tumours are sometimes observed in the neck a little before the commencement of this complaint, though probably depending rather upon accidental circumstances than upon the disease itself. Slave traders, however, appear to consider these tumours as a symptom indicating a disposition to lethargy, and they either never buy such slaves or get quit of them as soon as they observe any such appearances. The disposition to sleep is so strong as scarcely to leave a sufficient respite for the taking of food; even the repeated application of a whip, a remedy which has been frequently used, is hardly sufficient to keep the poor wretch awake."

Natives always seem to be fully aware of the importance of glands in the neck as a diagnosis of sleeping sickness. They call them "neck-stones," and in many parts of the West Coast, and in Northern Nigeria, the native doctors pretend to remove these glands by a superficial operation and scarification, which cannot have any influence on the course of the disease. The Mandingoes in the Gambia even cut the "neck-stones" of the boys to prevent the occurrence of sleeping sickness in later life! (Dr. E. Hopkinson.)

Robert Clarke, another Colonial surgeon, wrote a fuller

account in 1840 from observations he had made at Sierra Leone, and from that time onwards many English and French doctors became interested in and wrote of this disease, but all were agreed that it was confined to certain areas. Clarke stated that it was more common among the natives of the interior than on the coast, and that the disease was imported from the West Coast to other districts where it had not formerly been endemic. The slave traffic must certainly have greatly influenced the spreading of such a disease in Africa itself, and a very interesting record has been left us of 148 cases, studied by Dr. Guérin, a French doctor in Martinique, in the West Indies, among the slaves on the estates and in the hospital of Fort-de-France. These slaves had been imported from the West Coast of Africa, and only certain tribes, notably the Congo blacks, were liable to it. The disease *never* spread in the countries to which it was imported, and in such countries it completely died out when the slave trade was abolished.

Guérin says that sleeping sickness was considered by the Portuguese in Africa to be contagious, but in the island of Martinique it certainly was not so. No creoles ever developed it, though there were many cases among the Africans recently imported to the Antilles. If the disease were epidemic, he argues, it would cause more ravages among the slaves in the ships conveying them from Africa to the island, but he only heard of five such isolated cases. Of one hundred deaths on board these vessels, the ship's surgeon only attributed one death to sleeping sickness. A curious fact was that negroes developed the disease sometimes years after their arrival in the island, but never after ten years. More men than women were attacked, but then less than one-third of the imported slaves were females. The most susceptible age was from twelve to eighteen years. He gives a full account of the symptoms, but, as I shall mention them later, I will not quote them now. Like other early authors, he only describes the later stages, when the illness is apparent to all, and he therefore states that the diagnosis is always easy and that the prognosis is invariably bad. Of his 148 cases only one recovered. As most of these happened among slaves in domestic service he attributes their attacks to the change of diet and easier

life, and the greater strain upon their intellectual activity. Among others, he considers one of the most frequent causes to be grief, to which the negroes succumb when they are separated from their wives and home. It is easy to see how he came to this conclusion, for an invariable symptom of the disease is a certain moroseness or melancholy. Clarke, who had studied the disease in patients in their own country, thought it was due there "to smoking diumba, or Indian hemp."

Dr. Corré, a French naval doctor, writing in 1876 of his observations in Lower Senegal, attributes the disease to a kind of ergotism or scrofula and to the moral condition of the people. He tells us it decimated the little garrisons of black soldiers at Joal and Portudal, and he vigorously attacked the question, studying the conditions of the people, the climate, the water, and the food, and occasionally he comes very near the truth, for he notices that most cases occur near the water, and he maintains that the disease could be prevented by draining and cultivating the land. But the connection between the insect life of the country and the disease does not seem to have occurred to him. He cites many cases in which there are such manifestations as swollen glands, skin eruptions, nasal catarrh, etc. He visited all the principal villages of the country, and found cases of "Nelavane," the local name for sleeping sickness, in most. In some instances the villages had been left empty, the entire population having died or fled. From the Portudal district (in Senegambia) he reports: "This is the very centre of the Nelavane. The village of Dakann has been swept of its inhabitants by this disease, Nianing is only kept alive by the importance of its commercial situation, Warann and Portudal are bound to disappear, and M'Bout and N'Gaparou are equally threatened with destruction. Jungle grass, bush and forest are dense. The villages are ill kept and of wretched appearance, the population lazy and much addicted to drink, while their numbers are now much reduced."

Here, as elsewhere, he finds the unfortunate inhabitants mostly of miserable physique, with abscesses in the glands of the neck, conjunctivitis and enlarged bellies. Among them are cases where languor, headache and giddiness

suggest the later stages of sleeping sickness. He says the incubation period is very long, some individuals being attacked two, three, or even five years after leaving an endemic centre, and the natives do not consider a man from such a district safe till he has left it for seven years. Even the late stage of the disease, which he recognises, may last as long as two years, and death, which is invariable, is finally hastened by large bedsores on the back, because the unfortunate patient is unable to attend to his own cleanliness, and his friends consider they have done all that is needful when they have removed him to some little distance outside the village and have provided him daily with food, which he is often too weak or too somnolent to eat.

The popular belief is that the disease reached Senegal from some southerly country, and the chief of M'Bout asserted that it first appeared in Nianing when the blacks migrated from the South.

Corré, like other early writers, asserted that none but blacks ever had the disease, but he somewhat incredulously mentions that a missionary, Father Labat, who wrote a description of the people of the West Coast in the beginning of the eighteenth century, and yet never mentioned sleeping sickness, described the death of a European who had symptoms which strongly recalled those of Nelavane. Corré himself thinks he saw it in a Moor, and states that if this was a genuine case, these two were the first white men ever attacked. We have, unfortunately, abundant evidence now that this terrible disease is by no means confined to the negroes, for European missionaries, traders, doctors and others who venture into infected regions can and do become infected, and in almost every case of infection the malady has been fatal.

Although sleeping sickness has been a well-known scourge, as we have seen, among the natives of the West Coast of Africa, it was considered by early writers that the natives had a special tendency to it, for, although epidemics of it occurred from time to time, and villages were left deserted or full of dying and dead, it showed no sign of spreading far eastwards. It appeared to be confined to certain limited areas. Dr. C. Mense, the German author, found sleeping sickness as a widely-extended epidemic in

the navigable reaches of the Congo, and as far up as the Stanley Pools in 1885 and in 1887, nor had it been lately introduced into that region, for the natives knew it of old.

Many of the mission stations suffered exceptionally, and the danger of the infection is great. There is no doubt that the watchful chief of the village or the father of the family has learnt to recognise signs of the disease at a very early stage in the children, and the dread of it has amounted in some districts to a panic among the natives. They are ready enough to hand over stricken or suspected victims to the white man in the hope of ridding themselves of the burden, and so the infected come to congregate at the mission stations, and the mortality rises. Several stations on the Congo have had to be abandoned on account of the large number of deaths, amounting to 300 and even 600 among the youthful proselytes.

Writing in 1906, Dr. Mense reported that the number of deaths from sleeping sickness on the Congo within ten years amounted to at least half a million. In 1871 the first case of sleeping sickness appeared on the banks of the Quanza, in the Portuguese province of Angola, and since then it has claimed thousands of victims and prosperous villages have been left deserted. This outbreak induced the Portuguese Government to send out the first scientific Commission from Europe.

The careful investigations of that Commission have been of great and lasting use to later workers, although no definite conclusions were then arrived at as to the cause. When the later discoveries of Dutton, Bruce and Castellani threw new light upon the cause and course of the illness, the members of the Portuguese Commission re-examined the blood films of 12 of their patients to see if what they saw in them confirmed the conclusions which had been arrived at, and, looking at them with greater previous knowledge, they corroborated the solution which they had previously overlooked. The Portuguese Commission was the first to recognise the importance of gland swellings in the neck as a diagnostic help, for this is an inevitable symptom in the early stages, and one which had long been recognised by natives. It may now be said that all negroes with enlarged cervical glands in a sleeping sickness area should be con-

sidered infectious unless there are other obvious causes for the swelling.

For generations the disease seemed to remain within its limits, or at least to spread very slowly, and always on the West Coast, but the restless enterprise of the European can never be persuaded to leave things as they are. In his insatiable thirst for innovation and improvements, his desire for opening out new territories to commerce and civilisation, he must intrude into the privacy of Nature, and often enough civilised man innocently brings evils in his train undreamed of among the primitive savages whom he is trying to convert to Western ideas. With the opening of trade routes from the Congo basin, with the increase of steamer traffic up the river and round the great inland lakes, there is no doubt that the illness found every facility for spreading inland.

It is believed that the great English explorer, Henry Stanley, unwittingly helped to carry sleeping sickness from the centre of the Dark Continent to districts where it had never been known. In 1886 he was summoned from the United States, where he had acted as special correspondent to the *New York Herald*, to take command of an expedition for the relief of Emin Pasha, a German, who had held an appointment as Governor of the Equatorial Provinces under General Gordon.

Stanley had had an unrivalled experience of African travel. In 1871 he had made his first great journey from Zanzibar to Lake Tanganyika, a feat of much greater difficulty then than it is now, and had found Livingstone. With him he had explored the north end of the lake, and had conclusively proved that the lake had no connection with the Nile basin. He returned to Europe, but on the death of Livingstone he was fired with a desire to complete that great explorer's work, and to fill in some of the enormous blanks at that time still to be seen on the maps of Africa. His success in tracing the course of the Congo and in circumnavigating and fixing the outlines of the Victoria Nyanza, led to the founding of the Congo Free State, and ultimately to the general partition of Central Africa among the European Powers. Europe had felt great uneasiness as to the fate of Emin Pasha, and Stanley was the obvious man to accomplish the task of finding a white man in that vast and dark continent.

which no other man then living had explored so fully as he had done.

In Mareh, 1887, he started with a foree of 706 men—Zanzibar porters, Somalis, and Sudanese soldiers—to travel up the Congo to the relief of Emin Pasha, who was known to be somewhere in the Equatorial Provinee of Upper Egypt. At Yambuya, 1,300 miles from the sea, he divided his forees, leaving Major Barttelot in eommand of the rear column, while he himself, with five Europeans and a foree of 383 porters and attendants, started by forced marehes through interminable forests, swamps, hostile tribes, and every coneeivable diffieulty. Disaster overtook the rear column; Major Barttelot was killed, Jameson died, and only one Englishman, Bonny, survived. For months no news of Stanley reaehed England, and there was growing anxiety as to his safety, until news came that he had found Emin on the shores of Lake Albert Nyanza. It was a mission of goodwill, but mark what Dr. Mense, a great authority on sleeping siekness, states :—"Stanley's expedition for the relief of Emin Pasha, which travelled in 1888 from the Congo to the Nile, and whieh hired earriers from the Lower and Middle Congo, must eertainly have brought many infected men along with it to the Lake region, and possibly introduced the disease there. I myself was the witness of siek men regardlessly abandoned, of dead and dying, who marked the way even in the Cataraet region."

After Stanley had met Emin at Wadelai, near the north of Lake Albert Nyanza, he took him, after mueh delay and hesitation on the part of the Pasha, to Zanzibar. But the ex-Sudanese soldiers of Emin's province remained behind in a distriet to the west of the great lake. When Captain (now General Sir Frederick) Lugard arrived in Uganda in 1890, as the Representative of the British East Afriea Company, he found it advisable to have at his disposal a foree of armed men other than loeal natives. After he had deposed Kabarega, he came to Albert Nyanza in 1891 and reeruited a body of Sudanese, the remnants of Emin's army. From 400 to 500 able-bodied men were enlisted as soldiers, and they, with their rabble of 7,000 wives, children and followers, were brought into South Toro, and were placed under the newly appointed king Kasagama.

But they were a troublesome, lawless lot, and it was found advisable to move them again a year later, and place them under better control in Uganda and Busoga, and for some years there continued the recruiting of Sudanese soldiers who were brought to Busoga.

Sleeping sickness was then unknown in that part of Africa; none of the chiefs or missionaries had seen it, and when Dr. Albert Cook, of the Church Missionary Society, reported in 1901 that it had broken out in Busoga, the theory was generally accepted that it had been introduced by the settlers, many of whom had come originally from the edges of the Congo, where sleeping sickness has been endemic since time immemorial.

Dr. Hodges, the newly appointed Medical Officer for Busoga, at once investigated the epidemic, and found that the disease had existed in one district of Busoga for just six years, that many hundreds of natives had already died of it, and that it was confined to the shore of the lake and to the islands.

By 1908, seven years later, it had worked such havoc that it was reported that in this district alone it had killed 200,000 people out of a population of 300,000. Great Britain had spent much money and energy in establishing a good rule in this populous and richly cultivated country. She had completed a railway from Mombasa on the East coast to the shores of Lake Victoria Nyanza, and she contemplated a happy and prosperous people in the future, when she was confronted by this appalling disaster, a disease which threatened to exterminate the entire population, which baffled the skill of every medical authority, which was incomprehensible in its onslaught and in its course, and was inevitably fatal in its result.

The Discovery of the Human Trypanosome.

Before the year 1902 only one aspect of sleeping sickness was recognised, that which we have learnt to distinguish as the final stage of the disease, when the central nervous system is invaded, and when the most noticeable symptom is lethargy, accompanied by a staggering gait,

a tremulous tongue, and irregular fever. All those who were concerned in the study of the disease directed their attention, therefore, to this final stage.

It was attributed to various causes, some of which I have already referred to—home-sickness (among negro slaves), eating the root of the manioc, tropical heat, sun-stroke, intoxicating drinks, and other causes—but whereas the disease was widespread, these evils were purely local, and each was shown to be insufficient.

Later writers sought for a parasitological solution of the question, and Sir Patrick Manson, the founder of the London School of Tropical Medicine, thought he had solved the problem when he discovered a minute parasite, the *Filaria perstans*, in the blood of two patients from the Congo whom he studied, in conjunction with Sir Stephen Mackenzie, in the London Hospital in 1900.

The native of hot climates is a perfect museum of living parasites; he harbours in his blood, his intestines, and other organs so many different species that the diagnosis of his diseases is always difficult, because the special intoxication from which he is suffering may be due to many different causes.

When the two patients in the London Hospital died, a very careful pathological examination was made of their central nervous system by Dr. F. W. Mott, who discovered certain morbid changes in the spinal cord and in the brain, which have since been confirmed by other observers.

We now come to the first recognised case of human trypanosomiasis.

In the year 1901 an Englishman, the master of a Government steamer on the Gambia River, on the West Coast of Africa, broke down in health, and entered the hospital at Bathurst. His illness was at first thought to be malarial fever, a conclusion naturally arrived at in that climate, but as the fever resisted the action of quinine and other peculiar symptoms occurred the first diagnosis was abandoned. The special symptoms were irregular blushes on the skin, appearing on different parts of the body, some puffiness round the ankles, rapid respiration, a quick pulse and bad appetite, and the patient was losing flesh and colour, while the temperature rose intermittently and irregularly.

Dr. Forde, who examined his blood, found in it peculiar worm-like bodies, which were unknown to him. The patient was sent to England and admitted into the Royal Southern Hospital at Liverpool, where I had the opportunity of examining him, with Dr. J. E. Dutton, in August, 1902, and though I did not know what was the matter with him, I recognised it was a disease I had never seen before. As his health had improved by the autumn he returned to Africa, but he was very ill on the voyage out, and when he again came into the hospital at Bathurst his symptoms were very similar to what they had been before, only more marked. On December 18th Dr. Dutton made a further examination of his blood, and he then made the important discovery that the worm-like bodies noted by Dr. Forde were trypanosomes. The patient returned to England, and died there on January 1st, 1903.

It was a matter of the greatest importance to know whether the occurrence of the trypanosomes in the blood of this patient was merely a curious coincidence, or whether it marked the existence of a disease hitherto unclassified, namely, a human form of trypanosomiasis.

A trypanosome was next found in the blood of a native child in the Gambia settlement, and the discovery of a second case made it appear probable that the occurrence of the parasite was not merely a coincidence. Dr. Dutton gave to the trypanosome the name of *Trypanosoma gambiense*.

The Committee of the Liverpool School of Tropical Medicine was impressed with the importance of the discovery, and decided to send an expedition to Senegambia to make further investigations. The expedition consisted of Dr. Dutton and Dr. J. L. Todd, and they started their researches in 1902 both on human beings and on animals. The cases could not, unfortunately, be kept under observation, because the investigators had to travel about, and promptly lost sight of the people whom they had examined. They found trypanosomes present in the blood of seven out of one thousand cases examined. From our present knowledge we may assume that if they had punctured the glands of the neck in suspected cases they would have found a far larger number of people infected. Their account of the cases had

to be taken chiefly from the patient's own story, which is not always very reliable. The good-natured negro tries to give satisfaction by answering a question in the way he thinks you wish to have it answered, regardless of the facts. This the investigators soon discovered, and they had to rely altogether on their own examination and observation. They came to the conclusion that the disease, which they named trypanosome fever, or trypanosomiasis, was in natives a particularly mild disease, for many of those in whose blood they found the parasite appeared to be in perfect health, and none of them were very ill.

The relation between human trypanosomiasis and sleeping sickness was not at that time suspected.

This was how matters stood on the West Coast of Africa, and I must now go back to 1901, when reports reached the Foreign Office in London from His Majesty's Commissioner in Uganda of a widespread and disastrous epidemic of sleeping sickness in that country.

In April of that year the first cases were admitted into the Church Missionary Society's Hospital at Mengo, an institution which is under the charge of two brothers, Dr. A. R. Cook and Dr. J. H. Cook, and had existed for about five years. No cases of sleeping sickness had been seen in Uganda by these doctors before 1901. Of the first eight cases four came from Busoga, and the natives stated that it had been present there for some time, and was much more common than in Uganda. Before that year was out the cases had become so numerous that the hospital could not take them all in. Dr. Hodges, the newly appointed Medical Officer for Busoga, made an investigation and found that 20,000 people were already dead or dying of it in his district.

The Foreign Office consequently appealed to the Royal Society to send out a Commission to investigate the causes of the outbreak, and this Commission, consisting of Drs. Castellani, Christy and Low, arrived at Kisumu, the Victoria Nyanza terminus of the Uganda Railway, on July 8th, 1902. Dr. Low and Dr. Castellani had recently emerged from the postgraduate course of study at the London School of Tropical Medicine. Dr. Low and Dr. Christy received instructions to traverse certain infected districts, to collect

and examine specimens of blood, and to ascertain whether the theory of the connection between the presence of *Filaria perstans* in the blood and sleeping sickness was correct. The investigation of a new disease is one of the most difficult tasks possible, and it is often complicated, as in this instance, by mistaken hypotheses, which must first be cleared out of the way to make room for the truth.

Dr. Christy has given a most interesting account of the difficulties he encountered, and of his ultimate success in proving that the filaria theory was wrong. He travelled by canoe or on foot, mapping out the sleeping sickness areas and gathering all available information from medical officers and natives.

"All diseases are much alike to the native mind," he says, "and are regarded by him as visitations of evil spirits. The victim affects seclusion and his superstitious friends make excuses for him. If there is much mortality a movement is made to another district, the people leaving their houses and contents, as well as the standing crops. Should this occur often, the district becomes notorious and an epidemic may be brought to light. Only when the people are hard pressed and their medicine men have failed them do they apply to the white man for relief."

On most occasions he found the natives very friendly. Thus, after explaining his mission to the King of Ankole and his chiefs, runners were immediately sent to the petty chiefs to send in so many men from each tribe, and a large number of blood slides were collected for microscopic examination. But on some other occasions the natives resented his inquiries and investigations. He was enabled to determine the area of infection of sleeping sickness, and found that it was confined to a narrow strip of country surrounding the lake shores and the islands on the Lake Victoria Nyanza. The area of infection of *Filaria perstans*, on the other hand, extends in an entirely different direction, and he was therefore enabled to send to the Royal Society the first proof that the two diseases are not invariably connected.

While Dr. Christy and Dr. Low were making these studies in the infected areas, Dr. Castellani, at Entebbe, was busy examining the brains and spinal cords of people who had

died of sleeping sickness. He suspected a very minute *streptococcus*, which he found in the blood and heart, to be the cause of the disease, but in making his examinations on living patients he was surprised to find, on several occasions, trypanosomes in the cerebro-spinal fluid, which he drew off by lumbar puncture. He wrote a note on the subject, but hardly appreciated the value of the discovery.

The Royal Society in London had meanwhile determined to ask the War Office to lend them the services of Colonel David Bruce, of the Royal Army Medical Corps, as he was pre-eminently the man to carry out the investigation. Seven years earlier he had, in the most masterly manner, demonstrated that the *nagana* of Africa was conveyed from wild game to domestic animals by the bite of the tsetse fly, and his experiences in this research were of the greatest use in the actual difficulty.

Colonel Bruce and Dr. Nabarro arrived at Entebbe in 1903, and were met by Dr. Castellani, who reported what work he had done, and mentioned that he had found trypanosomes in five out of fifteen cases of sleeping sickness. This fact at once seemed to Colonel Bruce of immense importance, and he persuaded Dr. Castellani to continue his search for these parasites. Consequently, during the last three weeks that Dr. Castellani remained in Africa, it was found that 70 per cent. of the cases of sleeping sickness contained these trypanosomes in the cerebro-spinal fluid.

It is difficult to decide to whom the greater credit is due, to Dr. Castellani for his careful study which caused him to observe the very minute parasite, and for his care in making a note of the observation, or to Colonel Bruce for his skilful deduction that the trypanosome must be the cause of the disease. Bruce, with great generosity, gave all the praise to Castellani.

"This most interesting discovery of Dr. Castellani," he writes, "which was due to his introduction of the method of centrifuging the cerebro-spinal fluid in his search for the *streptococcus*, has been of the utmost possible value to the present Commission. It put them at once on the right track, and led to the rapid and easy elucidation of the ætiology of this hitherto mysterious disease. Without a knowledge of his observation they might have worked for

months in the dark, and, in truth, they might have returned to England still ignorant as to the true cause of the disease."

Subsequently it became known that the trypanosomes could be found in practically all cases of sleeping sickness, and never in healthy individuals. But the Commission was puzzled to find that trypanosomes in the blood did not always affect the health of the host. It was necessary to find out the subsequent history of such cases, and to determine whether they developed the more deadly symptoms when the parasite passed from the blood into the cerebro-spinal fluid.

Castellani considered that the trypanosomes which he found in cases of sleeping sickness differed somewhat from the *Trypanosoma gambiense* found by Dutton and others in Western Africa, so he named his parasite *Trypanosoma ugandense*, but other observers denied this difference, and eventually proved the trypanosomes to be identical by injecting them into animals, where they produced precisely similar effects.

Patients known to be suffering from trypanosome fever were kept under close observation, and it was found that their earlier symptoms gave place to those typical of sleeping sickness, and that they eventually died of that disease. It was thus proved that trypanosome fever is only the early stage of sleeping sickness, and is due to the same cause, the invasion of the *Trypanosoma gambiense* into the blood, and thence into the glands and the cerebro-spinal fluid.

From that time onwards the blood or cerebro-spinal fluid of each suspected case was examined for trypanosomes, and in 1904 it was found that an easier and surer method of diagnosing the disease was to puncture the glands of the neck with the needle of a hypodermic syringe, to suck up some of the fluid, and to blow it on a slide. When this fluid is examined under a microscope, the trypanosomes can often be seen in large numbers in early and late cases of sleeping sickness.

The Course of Sleeping Sickness.

The onset of the disease is insidious, for trypanosomes may be present in the blood for months, and even years,

before they enter the cerebro-spinal fluid and there give rise to the later and graver nervous symptoms. At other times the incubation is short, the symptoms appearing only a few weeks after the entrance of the parasite into the blood. In negroes the presence of the trypanosome in the blood appears to cause little or no discomfort, and the only symptom that gives rise to suspicion is a swelling of the cervical glands. They can be felt by the fingers, even when no blood test can be made. White people are more affected at this stage, for they suffer from irregular intermittent fever, the temperature rising for some days and then falling for some days; the pulse and respiration rate are also accelerated. There may be local œdema and an eruption on the skin, while anæmia, weakness, wasting and often headache are present.

Some cases end fatally at this stage without developing the later symptoms, but generally they continue for varying periods, and may last as long as several years, with occasional intervals of apparently good health.

The second stage, when the sleeping sickness proper is reached, is when the trypanosomes have invaded the cerebro-spinal fluid. As a rule, when they are found there, the patient is doomed, but even then death may be indefinitely postponed. Professor Todd reports the case of a negro in whose cerebro-spinal fluid trypanosomes were found in 1904, but four and a half years later he was still alive. A European, in whose cerebro-spinal fluid the parasites were found in 1906, was well a year later, when he married, and in October, 1911, he was still free from symptoms.

But these are exceptional cases. In most patients the second stage shows high temperature of a hectic type, rising every evening and falling in the morning, till, some weeks before death, the temperature falls below normal, and when this occurs both night and morning death is imminent. With this are found intense headache and a general degeneration of the mental condition of the patient. Negroes become morose, lose their volubility and prefer to sit alone, apathetic and dull. Their fellows regard them with suspicion, and if you inquire how the victim is, the ominous answer is given, "He sleeps." At this stage the patient may eat abnormally, so that he becomes sleek and looks

well nourished, and he may sleep to excess; often, however, he is not asleep, merely lethargic, and he can be roused to answer questions. There are tremors in the tongue and limbs, and occasionally epileptiform fits occur. The staggering, uncertain gait is very remarkable, and as the disease advances all the symptoms become more marked, and the patient cannot stand up or walk; he falls asleep in any attitude and sleeps profoundly, so that no noise or handling will wake him. If he asks for food he falls asleep before he has swallowed it.

Dr. Low tells us that his friends then prefer to remove him to the bush, where they lay him in a small reed hut and provide him with food, but give him no other attention. The patient lies there absolutely indifferent to his surroundings, asleep or half asleep, and can only with difficulty be roused for a moment. If he is removed into a hospital and treated, he improves for a little, even gets up and walks about, but very soon he will relapse, and his muscular weakness, wasting and drowsiness increase. The skin loses its lustre and eruptions may appear, with itching and bedsores. The tremors may become so great as to shake the bed on which he is lying, his drowsiness passes into coma from which he cannot be roused, the body becomes cold, and death comes to relieve him from his unhappy fate. The last stage usually lasts a month or six weeks.

But the disease varies, not only in races, but in individuals. The many cases examined by Drs. Dutton, Todd and Christy in the Congo did not exhibit the characteristic features of deep sleep or even continuous lethargy. The name sleeping sickness does not apply to these cases, and human trypanosomiasis has been suggested as a better name for the disease.

In the spring of 1909, by the courtesy of two French colleagues, I was fortunate in being able to see nine Europeans ill of this disease in Paris. In the infectious hospital attached to the Pasteur Institute I found eight Frenchmen and one Dutchman, all from the Congo, except one who came from the Niger in the French Sudan. All of these patients had been ill from one to three years, and had passed beyond the stage of fever and eruption, nor did they, at the time of my visit, harbour trypanosomes in the

blood or in the glands. Three or four of these patients showed such advanced disease in the nervous system that the prognosis was undoubted.

One patient had had two epileptic attacks, separated by an interval of six months; another, in spite of a gain in weight of 13 lbs., suffered from paralysis of his lower limbs, hyperæsthesia of muscles, and loss of sensation in his soles and feet and the lower half of both legs. A third had incomplete loss of memory and gradual failure of intellectual power, while a fourth, who had only been ill for eighteen months, laughed and cried without reason, and I was told that on arrival in Paris his mental symptoms were the most apparent, and though his neck glands were enlarged, no trypanosomes could be found in his blood, his glands, or his cerebro-spinal fluid. His mind cleared considerably under treatment with atoxyl, but, later on, paralysis of the right side of his body, loss of speech, and epileptic attacks occurred, and then trypanosomes were found in his cerebro-spinal fluid.

The hyperæsthesia I have mentioned as a symptom is an excessive or exalted sensibility, depending upon too great sensitiveness to impressions of the sensory nerves, or a too acute perception by the nerve centres of those impressions.

Attention has been called by Dr. Kérandel to the symptom of deep hyperæsthesia, which he discovered in his own person, and it is now called Kérandel's sign. He unfortunately contracted the disease himself, and thus describes the symptom :—

"Deep hyperæsthesia is one of the early symptoms of sleeping sickness; it appears in the second month, and becomes very evident in the third month. It shows itself when the soft tissues are sharply compressed, for instance, by a pinch or squeeze, and in blows accompanied by compression of the soft parts between a bone and a resistant surface. In the course of our daily occupations we unconsciously knock against many objects—articles of furniture, doors, stairs, &c.—without noticing any appreciable pain. In the case of trypanosomiasis the deep sensibility is exaggerated, so that these encounters cause a more or less sharp pain, not at all proportionate to their force. In this way I came to take

exceptional precautions to avoid touching the angles of doors, of furniture, the edge of my bed when I got into it, and legs of tables near which I sat. The fear of taking hurt by knocking myself had become a real obsession. The leg, forearm, and hands are most often involved. The pain is sometimes so great as to extort a cry. Contrary to what happens in the normal state, it does not come on immediately after the blow, but only one or two seconds later. It rapidly becomes then very sharp and piercing, but only lasts some seconds, and quickly gets less, disappearing after two to five minutes. This deep hyperæsthesia vanishes in a few days with atoxyl treatment.

"It is a symptom peculiar to trypanosomiasis. As far as my knowledge goes, it does not occur in any other tropical disease in this general way, and with these particular characters. It has, therefore, a great importance for diagnosis. It has already allowed us to discover, from information we received, the existence of sleeping sickness in a European sent home from the Congo two months before, and living in Paris without suspecting his disease. The symptom is easily observed. It is, of course, noticed by the patient himself, who often tells his friends of it, but forgets to mention it to his doctor."

The knowledge of this special symptom thus allows an early diagnosis to be made in infected Europeans, who can be removed from Africa for treatment at home before any serious degeneration has occurred.

Many of our most valuable studies on sleeping sickness have been made on European patients, because they have come under medical care at an early stage of the disease, and have been kept under careful observation. A very interesting case was that of Dr. Kérandel, to which I have already referred, who became ill in 1907, took careful notes of every symptom and of the effects of the treatment, and who had apparently recovered by 1910. Atoxyl does not seem to have contributed much to his recovery, which he himself attributes to intravenous injections of tartar emetic in Paris.

There are now fairly complete records of fifty European cases, the patients having been natives of Great Britain, France, Belgium, Italy, Germany, Norway, Sweden, Hol-

land and Portugal, and they had been residents in infected regions of Africa as missionaries, traders, soldiers, engineers and doctors. In all but five cases trypanosomes were found, either in the blood, or the glands, or the cerebro-spinal fluid, and in one case, when the parasites could not be traced, the fluid was injected into a susceptible animal, which subsequently developed the disease, thus proving the diagnosis.

In 23 of the fifty cases somnolence was recorded, and of these all but three ended fatally; when headache was present it caused intense suffering. In twelve cases there was remarkable change of character: three became irritable, and in two there were senseless fits of rage, two others acted irrationally, whilst two were emotional and wept without cause, and one was morose; seven suffered from delusions.

Outlook for the Patient.

The prognosis is always grave, for the great majority of patients die. The native does not usually come under treatment till he has developed the final and most serious symptoms, when his fate is sealed, and when the treatment can do no more than alleviate his sufferings and make his death less painful. Even if the negro presents himself for treatment at an earlier stage, and is apparently cured, he returns to the infected area, and his naked body is again a target for every hungry tsetse fly, so that he may succumb to a fresh infection at once.

There is no evidence that a previous attack of sleeping sickness gives any immunity.

But in the European the outlook is more hopeful. In most cases he comes to the doctor when he feels the first symptoms, and directly trypanosomes are detected in the blood he is sent out of the country and is safe from fresh infection. He submits to continuous treatment, and does not attempt to escape from his advisers, as the negro does when his condition begins to improve, and he yearns for liberty from hospital confinement.

Of the fifty recorded European cases, thirty-one are known to be dead, ten are still alive, and the fate of the remaining nine is uncertain, because they cannot be traced. Of those

who died, fourteen lived for a year or more after the disease was diagnosed, and five lived two years or more, one as long as six years. But no patient can be said to be cured until trypanosomes have, on several occasions, been proved to be absent in the fluids of the body. The parasites are difficult to find in cases where they are not numerous. They may be absent from the blood and present in the cerebro-spinal fluid, and *vice-versâ*.

The safest method of testing cases is to inoculate monkeys with the blood or cerebro-spinal fluid and watch the result. In the case of twenty-two patients in whose cerebro-spinal fluid no trypanosomes could be found under the microscope, 10 c.c. of the fluid was inoculated into monkeys, and seven patients were proved to be still infected. In thirty-eight others their blood was injected into monkeys, and eighteen of them were seen to be still infected.

Professor Todd does not consider that a patient can be considered cured until after eight years, because he has known instances in which the disease has recurred after eight years in persons who had apparently recovered. Though this seems excessive caution, it is difficult to fix a limit.

Dr. A. W. G. Bagshawe, Director of the Tropical Diseases Bureau in London, lays down as a working hypothesis : "If a patient has been under skilled observation for two years from the cessation of treatment, and has had for the whole time good health and freedom from fever and other symptoms, if careful examinations, made at intervals, have failed to find trypanosomes, and repeated inoculations of blood into susceptible animals are without effect, and moreover auto-agglutination of the blood cells is constantly absent, though we might express academic doubt as to his cure, we should, I think, feel fairly easy about him."

Formerly sleeping sickness was considered absolutely incurable, but this can, happily, no longer be said, provided that treatment is energetic and is begun early.

A large number of drugs have been used, but where a single drug has been tried the result has been disappointing, and a permanent cure has very rarely been affected. But it has been observed that a combination of drugs may be much more effective when the various substances, used by

themselves, have not been successful. Good results were obtained at Liverpool in 1906–7 by the use of successive drugs in preventing relapses of trypanosomiasis in rats which had been artificially infected, and it is now found that the combined treatment of atoxyl and antimony gives the greatest chance of success in the analogous disease of human beings. The fact that such a combination is effective can be best explained by the assumption that several chemical reactions go on side by side.

There is now a man under Sir P. Manson's care who acquired the infection in Rhodesia in September, 1909, probably from *Glossina morsitans*. He reached the Albert Dock Hospital in London on February 26th, 1910, weighing only 8 st. 6 lbs. Now, after two and a half years' treatment by atoxyl, antimony, or salvarsan, he has gained thirty pounds in weight, "and shows no sign of implication of the nervous system." Originally trypanosomes could be found almost every day in his blood, but powerful drugs seem to have banished them to a certain extent. They are still to be found at intervals of about twelve to seventeen days. He is now well enough to be a spectator of football matches, he enjoyed a day's skating at the beginning of February, 1912, and he can walk three miles without fatigue.

The most successful English case is that of a lady who apparently contracted the disease at the end of 1900. Trypanosomes were found in July, 1902, and now, twelve years after the beginning of the symptoms, she is reported to be in good health. Another lady, whose case was also reported by Sir P. Manson, is in good health more than ten years after the onset.

Many native patients have a great craving for meat, even when they are obviously nearing their end. This craving may be due to the stimulating quality of nitrogenous food, or because the sufferers have less fever than when on their ordinary diet of bread and vegetables. Captain R. J. C. Thompson, R.A.M.C., has lately been giving sugar to his patients in the Lado Enclave (Sudan), and reports that this addition to the rations certainly inspires content and improves the powers of resistance.

Discovery of the Carrier of Sleeping Sickness.

Having ascertained with some certainty that the presence of trypanosomes in the blood and cerebro-spinal fluid is the cause of trypanosome fever, which develops into sleeping sickness as the disease advances, Colonel Bruce and his fellow worker, Dr. Nabarro, proceeded to determine how the parasite enters the human body. They were struck with the limits of the geographical distribution of sleeping sickness, for they found it confined to the shores of the lake, the islands lying in the lake, and, as they found later, the banks of rivers. Natives informed them that any cases which occurred inland had always been imported from such regions, but the disease never spread away from the watered district, although there was constant communication between the natives living on the banks and those inland.

Where the disease was endemic it was generally supposed by the natives to be capable of transmission from one human being to another, but it was difficult to understand how the trypanosome could get out of one individual into another, and it was remembered that former authorities, writing from the Antilles and the West Indies, had stated that the numerous cases they had seen among imported negroes were all sporadic instances, and had never infected other people. The natives of French Guinea maintained that the disease was propagated through the bite of a fly, and Dr. Dutton and Dr. Todd examined two species of the biting flies of Gambia without succeeding in conveying trypanosomiasis to animals by means of the bite of these flies.

It seemed probable to Colonel Bruce, judging by his previous knowledge of the tsetse fly in Zululand, that the same insect might be the transmitter of human trypanosomiasis, although he was informed that the tsetse fly did not exist in the sleeping sickness areas. "A short search in the Botanical Gardens of Entebbe disposed of these objections," he tells us. He found large numbers of the tsetse fly, very similar to the *Glossina morsitans* of Zululand, which he had proved to be the insect carrier of trypanosomiasis to animals, and some native children were soon engaged to catch as many tsetse flies as they could find.

They brought many hundreds, and Colonel Bruce then invited the Prime Minister and the native Regents to meet the Commission and to have the matter explained to them.

The fly was immediately recognised as one known to them as "Kivu," and they stated that it swarmed along the shores of the lake. They were then supplied with butterfly nets, killing bottles and boxes, and they promised to have the flies of their respective districts captured.

The Bishops of Uganda also promised their assistance, and offered to enlist the help of missionaries. Every official and every missionary had a specimen of the tsetse fly sent to him with this letter :—

"Sleeping sickness in many ways is very similar to the fly disease of South Africa. It is caused by the same kind of parasite, and is possibly carried from man to man by some insect, as the fly disease is carried by the tsetse fly (*Glossina pallidipes*). A species of tsetse fly (*Glossina palpalis*) is also found in Uganda, especially along the shores of the lake and in the islands. It is possible that this fly acts as the carrier of the infective agent of sleeping sickness. If this is so, the disease can only occur in places where the fly is found. In other words, no tsetse fly, no sleeping sickness.

"In order to settle this question the distribution of this fly must be carefully worked out. To assist in this, would you kindly send collections of biting flies from your district, and answer the following questions :—

"(1) Is the tsetse fly (*Glossina palpalis*) found in your district? (2) In what kind of place is the fly found : marsh, banana plantation, bank of river, shore of lake, forest, bush, or open places? (3) When does it bite : during the morning, mid-day, or at night? (4) Is it numerous? (5) What animals does it bite? (6) Does sleeping sickness occur in the same place, distinguishing, of course, between imported cases and those which have been infected on the spot?

"If no tsetse flies are found in the district, please send a specimen of any of the various biting flies or insects known to the natives."

During the next three months the Commission received from all parts of Uganda 460 collections of biting flies.

As each packet arrived, the contents were divided into tsetse flies and other flies, and, if the parcel contained even

one tsetse, a red disc was stuck up on a specially prepared map over the place from which the parcel had been received. If the enclosed note stated that sleeping sickness was present in the locality, a red disc was stuck upon a similar map which had been prepared to show the distribution of that disease.

These two maps showed at a glance whether the distribution of sleeping sickness and of tsetse fly corresponded or not, and when the reports were complete it was evident that the correspondence was exact.

The fly was found to live exclusively on the shores of lakes and rivers where there is forest and dense undergrowth; on the other hand, where there is open, sandy beach, without shade, the fly never comes, and it never travels far from the water.

"It is on the densely wooded shore of the lake," writes Colonel Bruce, "that the half-naked natives of the mainland and islands meet in thousands to trade in fish, bananas, earthenware, &c. If the *Glossina palpalis* can act as a carrier of the trypanosomes of sleeping sickness, the circumstances could not be made more favourable than they are for the spread of the disease."

The evidence in favour of the tsetse theory was convincing, and only needed to be proved. It was therefore necessary to experiment on animals, and for this purpose monkeys were chosen, because they are easily fed, were easily procured, and they do not languish in captivity. Tsetse flies were fed on cases of sleeping sickness, and the cage containing them was then, at various intervals, placed upon the monkeys. The sleeping sickness patient did not appear to feel the bite of the fly, and the experiments succeeded in proving that the *Glossina palpalis* can convey trypanosomes from sleeping sickness patients to healthy monkeys.

Next, it was important to find out if the wild tsetse fly, caught and at once placed upon a healthy monkey, without first feeding it on a sleeping sickness patient, was capable of infecting the monkey. For this purpose flies were captured near the hut tax labour camp. "Men, to the number of thousands, come to Entebbe to work for Government for one month in lieu of paying hut tax. They live in loosely built grass huts near the shores of the lake." Tsetse flies

were caught among their huts and were brought to the laboratory, where they were placed upon healthy monkeys, and when the blood of these monkeys was examined later, it was found to contain trypanosomes. This experiment at once showed the authorities what a grave risk they were running in allowing the hut tax labourers to live so near the lake, for at the end of their period of work they would return home, many of them, in all probability, with the trypanosomes in their blood. Such cases, in fact, were reported, but as they had returned to districts where there were no tsetse flies, their disease was not conveyed to others for want of the intermediary carrier.

The fact that the tsetse fly is the necessary carrier of the disease solved the mystery as to why sleeping sickness did not spread in regions like the West Indies, where numerous cases were introduced. There were no testse in those countries to act as carriers, and therefore the disease could not spread from the sick to the healthy.

As a consequence of Colonel Bruce's experiments, segregation camps or villages were started in Uganda in December, 1906, and though the authorities cannot boast of recoveries from the disease, they have had the satisfaction of having removed many carriers of the trypanosome away from the fly areas, and the camps have been of distinct educative value in demonstrating that the relatives and attendants on the sick have not contracted sleeping sickness.

Trypanosomes and Tsetse Flies.

I have recorded how our knowledge of sleeping sickness has grown. and how the ignorance which hung about it was dispelled by the splendid work of Sir David Bruce and others in demonstrating that the disease is caused by the presence, in the blood, glands and cerebro-spinal fluid of the patient, of a certain minute parasite, the *Trypanosoma gambiense*, and how this parasite is conveyed from man to man by a tsetse fly, such as the *Glossina palpalis*.

Trypanosome is derived from two Greek words, *trypanon*, a corkscrew or boring instrument, and *soma*, a body.

Under this name are included organisms of the class

flagellata, protozoa with an elongated, somewhat fish-like body, with a *flagellum*, or whip, at their anterior extremity. The trypanosome moves with great activity, lashing its *flagellum*, which is the end of an undulating membrane or fin running down the whole length of the body. As far as we know at present, the typical trypanosome always inhabits the blood of vertebrates.

The first trypanosome was found by Valentin, of Berne, in the blood of a trout in 1841, and, later, other trypanosomes were found in frogs, rats, and other animals. Naturally their study assumed greater importance when it was found that certain trypanosomes were pathogenic, producing disease in the host, animal or man. The diseases thus caused are called trypanosomiasis.

In 1880 Evans discovered the trypanosome which causes the illness called *surra* in horses and camels in India, and in 1894 Bruce found the *Trypanosoma brucei* to be the cause of *nagana* amongst the horses and domestic cattle of Zululand. Bruce was the first to bring the pathogenic trypanosomes to Europe, where their study has engrossed the energies of many scientists.

These minute parasites are stained, preserved, cultivated, and inoculated into experimental animals, their life-history has been studied, and, as a result of all this work, discoveries of the greatest importance have been made, proving that these infinitesimal protozoa, needing the strongest microscope to make them visible to the human eye, play a terrible part of death and destruction in the animal and human kingdoms.

At least four diseases[1] which have worked terrible havoc among the cattle of India, Africa, or South America, are due to trypanosomes, and a great deal of study is still needed to complete our knowledge regarding them. But now that the devastating disease which we call sleeping sickness is known to be due to trypanosomes, these parasites have taken their place as of foremost interest in pathology, and the study of them in the tropics is as indispensable to the medical officer as to the veterinary surgeon.

[1] *Nagana*, *surra*, *mal de caderas* (disease of the hind quarters), and *dourine* (known also in Southern Europe).

The length of the *Trypanosoma gambiense* is about three times the diameter of a red blood corpuscle, and they differ considerably in appearance, some being long and slender, with a long *flagellum*, while others are shorter and broader with a short *flagellum*. As is the case with most trypanosomes, they multiply by longitudinal division, and this process may be repeated till the blood is swarming with them. In the blood of man they are, however, usually very scanty.

It is probable that the parasite enters the lymph stream directly it is introduced by the bite of the fly, and is carried to the lymphatic glands, which it inflames and through which it passes into the blood stream and cerebro-spinal fluid. We do not yet know how the trypanosome produces the pathological changes in its host which call forth the symptoms of the disease, though it probably does so by the production of a toxin.

The fact of a man having trypanosomes in his blood does not make him a source of danger unless there is present the insect which can convey the parasites from his blood to that of others. No danger is therefore attached to the importation of cases from Africa into Europe. The carrying agent is the tsetse fly, which is peculiar to Africa and Aden, and wherever the special tsetse called *Glossina palpalis* exists, it appears to be the sole agent. The distribution of sleeping sickness depends on its insect carrier, as is also the case with malaria and yellow fever.

The study of tsetse flies is of great importance for the material progress of vast stretches of Africa, for, while some species of this formidable pest have the power, as we have seen, of depopulating the regions where they reign, others can exterminate the domestic animals on which man depends, and thus make agricultural prosperity an impossibility.

There are now fifteen known species of *glossina*, and to those who visit equatorial Africa it is necessary to be able to recognise tsetse flies, and especially the *Glossina palpalis* and *Glossina morsitans*. Tsetse are very ordinary-looking, dark brown, blackish, yellowish brown, or yellowish flies, varying in length from six millimetres to 13 millimetres, according to the species, say $\frac{1}{4}$in. to $\frac{1}{2}$in. long. In some the hinder half of the body, the abdomen, is of a paler colour,

and marked with dark brown bands, but this is not the case in *G. palpalis;* this species is rather less than half an inch long, with an almost black body and a pale patch on the abdomen. Its dark appearance makes it easily recognisable. The abdomen cannot, however, be seen while the insect is at rest, because the wings are folded over it. These "brownish wings lie closed flat over one another down the back, like the blades of a pair of scissors, while the proboscis projects horizontally in front of the head." The mode of folding the wings and the prominent proboscis are the two chief distinguishing features in the fly, which has otherwise nothing at all remarkable in its appearance. Unlike most flies, the tsetse does not lay eggs. The female fly is reproductive for at least three or four months, and about eight to ten times during her life she develops in her body one larva or maggot, which she drops in a shady place near water, away from swamps. She therefore takes much more highly organised care of her offspring than does the ordinary insect which lays its eggs in a suitable place and leaves them to hatch into larvæ by themselves.

The new-born larva creeps into the loose, dry soil to a depth of a half to a little more than one inch, immediately becomes dark in colour, and after a few hours changes into a pupa. When it is first born it is a yellowish, footless maggot, with a deep depression at one end, between two black, granular prominences, or lips. The pupa is dark brown in colour, and the prominent lips are as noticeable as in the larva. The pupa stage lasts from 17 days in warm weather, to as long as 72 days in the two cold months of the year, although the difference of temperature is only very slight. At the end of that time the perfect fly emerges. Each female thus produces in her lifetime the relatively small number of not more than nine descendants.

Larvæ are found in great quantities in sandy soil or crumbling vegetation, on the shores of a lake or river, shaded to some extent by shrubs or trees. They are generally found about five yards from the high water mark, and never more than 15 yards away. As many as 800 pupæ were collected by natives from the shores of a lake in one day. They have also been found within the leaf sheaths of the oil palm, in the forks of branches of trees up to ten feet

from the ground, in the crevices of rocks, and at the bases of banana plants.

The fly is seldom found at a high altitude, probably because the colder air is unsuitable to its development. Where rivers run through dense forest and where the sun does not penetrate, they are not found, but they are seen round the small, shallow pools which the natives have dug.

The *Glossina palpalis* is generally able to get as much animal blood as it wants, and it cannot live without it. Its habitat is undoubtedly influenced by the presence of animals which live by the water's edge and the vicinity of natives. It has been noticed by those who have studied the fly, and who were catching as many specimens as they could, that sometimes a river would appear to be free of flies till the searchers reached a landing stage or other point frequented by natives, when large numbers were at once found. Flies will congregate at a ford or near a group of native huts, by the water's edge, flying to these points from a considerable distance, for they prefer human blood to that of other animals. They will follow native carriers some hundreds of yards, and isolated flies have been seen in huts nearly a mile from the water, where human traffic and sheltered scrub have tempted them from their usual haunts. This habit of following travellers is one which is extremely dangerous in the spread of sleeping sickness. A number of flies can be seen to follow a party of natives flitting through the bush, and if the party meets another coming from the opposite direction, some of the flies will leave the first group and attach themselves to the second.

There is no distance flies will not travel in boats up and down the rivers and on the great lakes, and they will fly some little distance to meet a boat and settle upon it. They are often seen to enter a railway carriage, approaching the train as it stands at the station. They perch on the window sill, then fly to the floor and creep under the seats. European women in railway carriages are thus easily attacked, through their thin stockings, and they are therefore urgently warned to protect themselves by wearing putties or gaiters. *G. palpalis* has been found in the railway station in districts far removed from the fly regions,

whither they had doubtless travelled many miles inside the railway carriages.

Professor Koch, who made valuable studies of sleeping sickness and the tsetse fly, was at one time convinced that the blood of the crocodile was the staple diet of the fly. His researches were made on Victoria Nyanza, where crocodiles are plentiful. Other observers agreed, and Koch thought he had put the matter beyond doubt when he discovered in the blood which the flies had sucked a parasite peculiar to the crocodile. There is no doubt that the tsetse feed largely on that reptile in certain regions, but there are many rivers where there are no crocodiles, and yet these flies swarm.

They probably feed on all or almost all mammals, some reptiles, and even fish. It has been observed that one species of tsetse, the *Glossina morsitans*, can exist for a considerable time without food, and this probably applies to other species, but it is doubtful whether, in the absence of food, the fly can reproduce itself.

Tsetse flies probably have many enemies, as all wild creatures have, but we are very ignorant on this point. The adults are probably eaten by birds, lizards, spiders, or a mantid (H. H. King), and the empty pupal cases have been found with a small hole in the side, as if some parasitic insect had devoured the contents. But their bitterest enemy should be man, and when he has found out all that there is to know about the breeding grounds and haunts of these deadly pests, he must set himself to wage a war of extermination.

Men are in danger of being bitten wherever they are in the habit of congregating, and where the flies expect them; for instance at cross-roads, where the natives sit and rest, at fords where they meet and talk, in the paths leading to the villages, under the shady tree in the hamlet where the inhabitants gossip, in the road leading to the village water supply, and in the traveller's tent, where the fly enters and conceals itself under the bed or in any other hiding place.

Glossina palpalis gets up with the sun, becomes torpid and less active in the heat of the day, and disappears towards evening. Some observers maintain they have seen it biting by moonlight, but this must be very rare. It is the old-

established custom, in many parts of Africa, to travel, if possible, by night.

The flies prefer the shade, but wind at once drives them to seek shelter. Their swift, irregular flight is familiar to the African traveller. Some tell you that their approach is almost noiseless, but others say that the peculiar buzzing sound they make, in flying, makes it easy to hear them on the wing. The word Tsetse is formed from the resemblance to the sound made by the fly. (Similar onomatopoetic words are cuckoo and peewit.)

When they are hungry they persistently return to the victim they have selected to bite, even after they have been driven away, although in this respect they are less tiresome than *Glossina morsitans*. When a white man is travelling through a fly region accompanied by blacks, his light clothing and fair skin protect him, but it has been noticed that if he puts a dark wrap over his shoulders the flies readily settle on that. Of course the almost naked black man offers a more tempting bait to the hungry fly, but the fact that they prefer a black to a white surface may be accounted for by the laws of natural selection, the instinct of the dark insect driving it to seek a place where it is less conspicuous. Captain Ensor writes:—"In my opinion white clothing confers the greatest degree of immunity from the attacks of these insects." This preference for dark colours is not peculiar to *Glossina palpalis*, but is marked in the case of all blood-sucking insects.

When the fly feeds it spreads its legs out to bring its body nearer to its host, and then buries its proboscis deep into the skin. A sharp prick is felt at this moment, but there is very little irritation to follow, and the natives pay no attention whatever to the flies, for they feel them less than they do the mosquitoes. If the fly is not disturbed it gorges itself with blood, and its capacity for extension is great. Having fed, it seeks the shelter of a bush or long grass, generally resting on the earth in the shade, and it may remain many days without food. Some writers say that it seldom attempts to bite through clothing thicker than thin stockings, but on the Congo it has been seen to bite through *khaki* breeches.

Until quite lately, it was believed that the tsetse fly

carried the infection only by mechanical means, but for the last two years we have known that, when the *Glossina palpalis* has drunk the blood of an infected animal or man, its bite remains harmless for a period of 18 days, after which it may become highly infective, and be capable, for an unknown period, of conveying trypanosomes to healthy people. During the stage of non-infectivity it was assumed that the parasite was going through some cyclical change within the body of the fly. The British Sleeping Sickness Commission has recently investigated this question in Uganda, and made the interesting discovery that the fly does not become infective until the trypanosomes invade the salivary glands, which they do in the short stumpy form similar to that which is found in the blood of vertebrates, and which is called the "blood type."

Very minute examination of laboratory-bred flies, fed on infected animals, showed that in all the flies trypanosomes could be found for three or four days after an infective feed. But in 92 per cent. of the flies trypanosomes disappeared after six or seven days. In the remaining eight per cent., however, trypanosomes persist and increase in enormous numbers. Why the parasite dies out in some flies and survives in others, is at present unknown. Their presence does not appear to inconvenience the fly in the slightest degree.

Some pupæ of *G. palpalis* were sent from Victoria Nyanza to London, and though they reached here in the unfavourable month of December, they hatched successfully into tsetse flies in the Insect House at the Zoological Gardens.

By examination of every part of the alimentary canal it was found where the parasites are most numerous, and that, except immediately after a feed, the proboscis is free from them. There are no trypanosomes in the salivary glands at first, but on the 25th or 26th day they appear there, and assume their normal blood type. A fly biting at this stage is in the highest degree infective. But during the development stage, although the gut may be swarming with parasites, the fly is not capable of communicating infection. As to what actually takes place within the insect, we are still ignorant, but the researches of Professor Kleine and others will doubtless solve this mystery. It is probable that when once a fly becomes infective, it remains dangerous for the

term of its whole life, which may possibly extend to twelve months.

We have seen that the geographical distribution of sleeping sickness corresponds in Central Africa with the distribution of *Glossina palpalis*, and it was believed that this fly acted as a carrier of the disease to the exclusion of all others. But it has lately come to be known that sleeping sickness occurs in Rhodesia and some other parts of Central Africa, where *Glossina palpalis* does not exist. Careful preventive measures had been in existence in Rhodesia for some years, because it was known that there were cases just over the border in the Congo State territory.

In 1907 it was found that *Glossina palpalis* existed at the south end of Lake Tanganyika, and it was recommended that the movements of natives should be restricted, the border patrolled, villages moved away from the edge of the water, and the shores cleared of underwood, where the flies shelter. These precautions were adopted, the river was closed for crossing except at one point, the shores of the lake were cleared, and natives moving in or out of the *G. palpalis* area were only allowed to do so with permits. All cases of sleeping sickness were segregated in camps in charge of a medical officer, far removed from fly-haunts; but, while these arrangements were in preparation on the west shores of Lake Tanganyika, some infected natives escaped over the border into German territory. The Germans at once made arrangements to return such undesirable immigrants, but when other cases escaped into Belgian territory, difficulties arose. Unfortunately the lack of co-operation on the part of the Belgian authorities makes all legislation to guard against sleeping sickness extremely difficult where our territories adjoin. On the banks of the River Luapula, for instance, it is useless for us to expend much energy and money in clearing our side and in moving natives, when fresh villages are springing up on the opposite bank, many of them peopled by refugees from our side. These river-side villages, inhabited by fisherfolk, who are the greatest sufferers from sleeping sickness, are a continual menace to the natives we are trying to help, and a source of constant temptation to them to return to their old haunts.

Dr. Kinghorn and Dr. Montgomery, who were waging

war against the disease in North East Rhodesia and Nyasaland, wrote:—"We have seen enough . . . to make us realise very fully the great importance of international co-operation in dealing with sleeping sickness. However good a system of fighting the disease may exist in one country, its efforts are sure to be retarded if the neighbouring countries remain apathetic. When the authorities in Rhodesia commenced to isolate the infected, some of them, and in one or two cases, whole villages, immediately decamped over the border, where they not only constituted a source of danger to their new country, but remained one to that which they had left, for the probability existed that they would find their way back to their old villages as soon as they thought that the vigilance of the authorities had relaxed."

Yet in spite of these and other difficulties, nearly 12,000 people have been moved away from the lake shores and river, some to a distance of 15 miles, and it has all been accomplished without using coercion, the natives willingly handing over their canoes to the Administration. When anyone passes from a non-infected to an infected area he has to pass through one of six administrative stations, where the officers are responsible for checking communication, whenever possible.

But, notwithstanding these precautions, admirably planned and conscientiously carried out, cases of sleeping sickness appeared, and these were occasionally reported from districts where the *Glossina palpalis* was known to be not present. Two other species of tsetse fly, therefore, came under suspicion, the *G. morsitans*, already known to be the carrier of *nagana*, a trypanosomiasis of animals, and the *G. fusca*. *G. morsitans* was reported to be increasing in the affected districts, and at the same time sleeping sickness had spread within the last three or four years far enough to come in touch with other species of tsetse, to districts where the *G. palpalis* does not exist.

Towards the end of 1909 reports were sent to the Sleeping Sickness Bureau in London of eight cases of trypanosomiasis in man, some of which became infected in Nyasaland, in Portuguese East Africa, or in Rhodesia, south of a known *G. palpalis* area. The European cases were valuable evi-

dence of the fact that people could become infected in these districts, for uncorroborated native statements can seldom be relied upon. The authorities were now faced with two alternatives, either (1) the *Glossina palpalis* existed further south than was generally supposed, or (2) human trypanosomiasis can be transmitted by other tsetse than *G. palpalis*.

Glossina fusca is rare in Rhodesia and Nyasaland, and does not attack man to any great extent. *G. morsitans*, on the other hand, is a vicious and persistent biter, and is present in enormous numbers. Circumstantial evidence thus implicated the *G. morsitans*, and only laboratory evidence, exact and convincing, was needed.

In April, 1911, Dr. M. Taute began some important experiments on monkeys at Niansa, which is on the shore of Tanganyika, and free from all species of tsetse fly. *G. morsitans* pupæ, derived from laboratory-bred mothers which had been fed daily on sheep, were sent to Niansa, and when the young flies hatched out, they were fed on monkeys which had been inoculated a short time before with a teaspoonful of blood taken from three sleeping sickness patients in the neighbourhood. In October Dr. Taute was able to publish his results, which were that *G. morsitans* can play the part of a real host, and not that only of a purely mechanical transmitter, of the parasite of sleeping sickness. He found that the development of the trypanosomes in the body of *G. morsitans* takes about the same time as the similar process in *G. palpalis*.

Further, on October 20th, 1911, a cablegram from Livingstone, Northern Rhodesia, announced that Dr. A. Kinghorn had succeeded in transmitting *Trypanosoma rhodesiense* by means of *G. morsitans*.

These laboratory experiments do not, however, yet prove that similar transmission is of common occurrence in nature.

The trypanosome found in Rhodesian cases is slightly different from the *Trypanosoma gambiense*, and has been named the *Trypanosoma rhodesiense*, but although the species is distinct, the fatal effect on the patient is similar.

The symptoms considered of most value for diagnosis in Rhodesia are fever, puffiness of the face and eyelids, tremor of the tongue, general shakiness, a vacant expression and

slowness of movement and speech, with enlargement of the glands of the neck.

In 1910 Dr. J. W. W. Stephens noticed in the blood of a rat, which had been inoculated with sleeping sickness from a patient then under treatment in Liverpool, that the trypanosomes showed some peculiarities of structure not seen in *T. gambiense*. He and Dr. H. B. Fantham eventually arrived at the conclusion that there is a new species of trypanosome in man which also causes sleeping sickness.

The new *T. rhodesiense* is characterised in sub-inoculated animals by the presence of a posterior nucleus, in certain of the short or stumpy forms; the nucleus may be quite posterior and behind the blepharoplast. The conjecture of a new trypanosome was confirmed when cases of sleeping sickness were reported from a part of N.E. Rhodesia where no *G. palpalis* is known, but where *G. morsitans* abounds. Since then Dr. F. K. Kleine has recorded the existence of sleeping sickness in German African territory where only *G. morsitans* is met with. It is agreed that the new species in laboratory animals is distinctly more virulent than any strain of *T. gambiense* yet described.

In N. Rhodesia about 16 per cent. of the wild game examined are found to be naturally infected with *T. rhodesiense*, while at least 37·5 per cent. of the buck in the Luangwa Valley harbour trypanosomes of one or more of six species. It is now suggested as a possibility that the new trypanosomiasis has existed, in animals at least, in Rhodesia and Nyasaland from time immemorial. Since 1908 there have been diagnosed 47 cases of human trypanosomiasis in a limited area of Nyasaland, all apparently due to the bites of *G. morsitans*.

The importance of the confirmation by Dr. Kinghorn is evident, for it opens out the possibility of the spread of this terrible disease to vast regions formerly considered safe, and it has roused investigators to the greatest activity, and all of us to justifiable anxiety concerning the fate of our great African colonies.

Wherever *G. morsitans* is found, it exists in much greater numbers than the *G. palpalis*, and its distribution is much wider, extending over hundreds of thousands of miles. We

know the havoc it works among the domestic animals by infecting them with *nagana;* if it is now found to have the power to convey sleeping sickness to man its powers of mischief are enormously increased. Whether the *G. fusca*, and possibly other tsetse flies, must also be implicated, remains to be proved.

So much prophylactic work has been carried out in recent years by anti-toxic serums or vaccines, which are the resistive productions of an immune animal which we inject into man to make him able to resist the attack of the particular poison he expects to receive, that it might be hoped that some such method of fighting sleeping sickness could be discovered. But in protozoal infections, such as that of malaria and sleeping sickness, this treatment appears to be ineffective, because the parasites learn to tolerate the injected antibodies, and their multiplication is not checked.

Measures of Prevention.

What the authorities have so far chiefly aimed at is to restrict the infected human beings and to withdraw them from the reach of tsetse flies. We know the fly to be merely a harmless pest till it has drawn infected blood, and if trypanosome-infected hosts can be kept away from the fly, it will continue to be harmless. But the fly, although limited to definite areas, inhabits some millions of square miles in tropical Africa, and feeds chiefly on natives who are quite indifferent to its bite and apathetic about the consequences. Whether their passive resistance to all preventive measures is due to fatalism, or to an entire want of faith, or to idleness, or, possibly, to all three of these causes, it is difficult to say; but it is a task requiring almost superhuman perseverance, courage and patience to help those who have no desire whatever to help themselves.

A constant source of danger at present is that when the native knows he is infected, he often leaves his own village to wander many miles for treatment at the hands of some specially-gifted magician, and in this manner the disease is carried into new regions. Such a patient is a source of

danger whenever he comes to drink or bathe at the water's edge, where flies await him.

If it were possible to return to the former conditions of life in Africa, when each tribe was at war with its neighbour, and no man ventured more than a few miles from his native village, these villages, should they be infected, would in themselves become segregation camps. But under the blessings of tribal peace and dawning civilisation, all this has been altered. Confirmation of this comes from H.M. Consul-General at Dakar, in Portuguese Guinea, who wrote in 1910 :—"Sleeping sickness exists in those parts of the hinterland that are favourable to the existence of the tsetse flies; but, curiously enough, it does not appear to be spreading as in other parts of Africa. Perhaps one of the reasons for this is because the means of modern communication, which are so rapidly finding their way into Africa, such as railways and steamboats, do not exist in the interior; hence the native population is more or less stationary."

But we cannot go back to primeval conditions and customs, and we must direct our attention to checking the extension of the disease. This must be done by dealing with (1) the fly which carries the trypanosome; (2) the persons who harbour the parasite in their blood; (3) the trypanosome itself. The fly must be attacked in its haunts, its pupæ must be found and destroyed, and the cover the fly needs must be done away with. The development of the soil will add to the prosperity of the people, and will banish the fly. Where possible, the land surrounding villages should be put under cultivation, and cotton, ground nuts, maize, and other crops should be planted.

While praising fly traps, Dr. A. Balfour mentions a limited fly belt in the Sudan, about twenty miles long and three or four miles in breadth. The fly is the *G. morsitans*, which here haunts the neighbourhood of wells. "This limited and peculiar distribution is said by the natives to be due to the fact that the fly was intentionally brought here from the river for purposes of revenge! This may or may not be true, . . . but certain it is that at the present time the natives trap the fly in gourds containing

blood as a bait, and then liberate them in spots where the cattle or horses of their enemies are grazing or are collected together. The trap is a spherical gourd with a hole cut in the top. It is half-filled with blood, and carefully watched. As soon as a number of flies have entered it in quest of food the native rushes forward and claps his hand over the aperture. He then closes the hole in some more permanent fashion, and carries off the flies in triumph for the future discomfiture of those with whom he has a feud. This native custom would certainly seem to indicate that a blood trap is a feasible method of dealing with one of the greatest pests from which Africa, the land of pests, has ever had to suffer."

Failing the extermination of the fly, which is an almost impossible task, considering the area covered by it, healthy persons must either be protected from its bites or taken out of its reach. Infected persons who have the trypanosomes in their blood must not be allowed access to fly regions, and they must be treated by remedies to destroy the trypanosomes in their blood.

To all these means of prevention and cure workers in Africa are directing their attention. A great deal of clearing of waterside vegetation has been done, and the planting of crops, obnoxious to flies, has, in some cases, been successfully tried. Thus, Dr. Lichtenheld reports that at a place near Sadani, *G. fusca* disappeared as soon as the ground was brought under cotton cultivation. Ground nuts and sweet potatoes might serve the purpose, but would suffer from the depredations of the hippopotami and the wild pigs.

Boat traffic up and down the river is a constant source of danger, for, as I have said, the fly will follow a boat for many miles and rest on it, and the authorities find that they can do no more than concentrate their efforts on landing stages, dipping places, fords and camps, where they can at least greatly diminish the number of flies, because, as we have seen, they are most numerous at such human resorts.

Great stress is laid also on the necessity of clearing the banks of streams crossed by railway bridges, and the neighbourhood of railway stations, and on trade routes properly

cleaned camps must be constructed and kept in order. In the German colonies the authorities have concentrated their attention chiefly on deforestation as a preventive, for the destruction of flies by this means is a guarantee of no fresh infection. The effect of this has been shown in Senegal, where the region of sleeping sickness and *G. palpalis* ends abruptly where deforestation has been carried out. The streams have dried up in consequence, and the flies have abandoned the district. Though disastrous to the country, deforestation seems preferable to the wholesale deportation of natives.

It has been suggested that jungle fowl should be introduced to find and devour the pupæ ; but there is no guarantee that they will prefer these to food more easily found, nor that they will .be spared by the wild beasts of the country.

River or lake-side natives usually spend all their time fishing, unprotected by any clothes, and they are constantly being bitten by infected flies. The mortality from sleeping sickness among them is higher than among any other class of natives. The only effective measure of prevention in their case is to remove the whole village as far away as possible from the water-side, to a distance of at least some miles, and to provide the inhabitants with a fresh occupation.

This has been done to a large extent. The rapid spread of sleeping sickness in Uganda was due chiefly to the habits of the natives on the coast and islands of Lake Victoria Nyanza.

In spite of their lack of interest in the subject, natives must be instructed about the disease and the dangers of the fly. Missionaries, traders and officials can help to a great extent by constant and reiterated teaching, and natives should be taught to wear more clothing in order to protect their bodies from bites. The relative immunity of the chiefs in Uganda is no doubt due to the fact that they are fully clothed. But it is no use hoping that the natives will learn from experience and observation, for if it were possible at all, the time it takes to get such a lesson into the native mind is too long. Considerable native teaching on the subject has, however, been carried out in the Uganda Pro-

tectorate, where the natives are amenable and relatively intelligent, and where they have learnt to co-operate to a considerable extent with Europeans in preventive measures.

Speaking of the native, Dr. Bagshawe says :—"He is by no means a stupid person where his own interests are concerned, and if he can be led to see for himself the means whereby he can avoid the disease and the simplicity of those means, he will himself take the necessary steps. It is recorded from various parts of tropical Africa that the natives know that their cattle die if bitten by the tsetse flies; it should not be difficult to induce them to apply the same reasoning to themselves."

History shows that in some parts of the Sudan former riverside inhabitants removed their villages from the banks to a considerable distance inland, apparently to avoid malaria. If the natives to-day fully realised the danger of the fly, which must live near the water, they might be induced to be equally prudent.

It is necessary to keep healthy persons away from the fly, but it is far more necessary to keep the infected people from being again bitten, for from their blood the fly receives a new supply of trypanosomes, wherewith it infects healthy people. For this reason the sick must be segregated in camps removed from the range of the fly, and the help of the native chiefs must be called in. They can detect early cases long before they have become evident to the European, and in fly areas an examination of all the inhabitants of the village should be made by gland palpation. It is a mistake to use compulsion in segregating the infected, as this leads to concealment of cases and to the running away of patients under treatment from the camps. It is obvious what patience, tact and forbearance are demanded from those who carry out the difficult task of searching out, isolating and treating sleeping sickness cases. As Thiroux remarks, "If you ask the village chief if he has any sick, he invariably answers that he has none." You must teach him first to co-operate in your work, and even then you must rely chiefly upon your own observation.

There should be no recruiting of soldiers, carriers or labourers from infected areas, and many observers consider

that all Europeans working in sleeping sickness districts should be periodieally examined for trypanosomes in their blood.

Present Research Work.

Important investigations are being carried out under the re-eonstituted Sleeping Sickness Commission in Central Afriea appointed by the Royal Society, eonsisting of Sir David and Lady Bruce, Captain A. E. Hamerton, D.S.O., and Major D. Harvey (all of the R.A.M.C.), to find out the reason why, although man and his domestie animals have been removed from the shores of the Lake Victoria Nyanza for some three years, *Glossina palpalis*, eaught on the north shores of the lake, still eontinues to infect susceptible animals with sleeping siekness when allowed to feed on them for experimental purposes. Their prime objeet is to investigate the part played by African fauna in the maintenanee and spread of sleeping siekness.

The effeet of the depopulation of the eountry was to make a two-mile area on the north shore of the lake practieally a game preserve, frequented by many kinds of antelope, hippopotami and wild pig. The late Commission set themselves the task of finding out whether this game, and especially the antelope, were capable of harbouring the parasite, being thus a perpetual reservoir from whieh the fly could get fresh infective material. Very eomplete experiments were carried out, and it was found that antelope are very readily infeeted with trypanosomes from flies previously infeeted with human trypanosomiasis, and that the blood of these artificially infected antelope again infeets other suseeptible animals if the *G. palpalis* aets as an intermediary carrier. In no single ease, among many animals experimented on, was the health of the antelope in any way affeeted. From a paper published by the Royal Soeiety in February, 1912, we learn that one of Sir D. Bruce's artificially infected antelopes still eontains, after 327 days, *Trypanosoma gambiense* in its blood.

It has now been proved that antelope living in fly areas in N. Rhodesia and Uganda are naturally infeeted by the

two human trypanosomes of sleeping sickness. This is a sufficient explanation for the continued infectivity of the fly round the lakes. It is important to find out whether other wild game can, and do, act as a host of the parasite. It has already been suggested that the wild game in sleeping sickness areas should be destroyed, but the British Government is unwilling to authorise any such wholesale extermination of animals, which might be wanted for food, until it has been more satisfactorily proved that the game are the *chief* reservoir of the parasite. Livingstone, writing nearly fifty years ago, on his expedition to the Zambesi, of the loss of his animals caused by the tsetse fly disease, says: "The destruction of all game by the advance of civilisation is the only chance of getting rid of the tsetse."

But Livingstone was unaware that the tsetse, when deprived of big game, can adapt itself to make use of man as its ordinary food.

The Sleeping Sickness Bureau, which has now been merged in the Tropical Diseases Bureau, had its origin in the International Conference on Sleeping Sickness, which was held in London in June, 1907, and March, 1908, to concert measures for the control of that disease. It was proposed at this conference to found a central international bureau "to extract and circulate all new literature on sleeping sickness," but the project fell through because the delegates of the various countries could not agree as to the seat of the bureau, nor could they all see the necessity for its existence. Thereupon Lord Elgin, then Colonial Secretary, established a British Bureau, to be maintained by Imperial funds, with a contribution from the Sudan Government, under the able directorship of Dr. Bagshawe, who had had practical experience of sleeping sickness in Africa. This bureau issued monthly bulletins, giving an account of current work in the field and laboratory on all trypanosome diseases, and these have proved extremely helpful to investigators. The circulation of the bulletin reached 1,100 copies, of which about half went to Africa. In addition, the bureau published maps of distribution of sleeping sickness and tsetse flies, an exhaustive bibliography, and a popular pamphlet on the means of prevention of sleeping sickness,

and has formed a library which already contains some 330 books and 1,500 pamphlets relating to sleeping sickness and diseases allied to it.

Every fresh discovery tends to increase the complexity of the problem how to deal with the question of prevention. It is now known that the fly remains infective after feeding on infected blood for 96 days, and possibly for the entire course of its life; that not only the *Glossina palpalis*, but also the far more plentiful *Glossina morsitans* is implicated; and now we must assume that an inexhaustible supply of infective material can be drawn by both these flies from innumerable reservoirs among wild game, and also among cattle and other domestic animals, which are known to be potential reservoirs, because they can be infected so easily by experiment.

Dr. E. Hopkinson, of the Gambia Medical Department, is not alone in thinking that native races may acquire some immunity against sleeping sickness. If this is so, it would partly explain the virulence of the disease when first discovered in a country, also the diminution of the number of cases in Gambia, where it is thought to account now for only one per cent. of all diseases, and where the natives agree that the malady is much less frequent than in the time of their forefathers. Cattle, too, are said now to live and thrive in Gambia in a way which used to be impossible.

But active work is going on in many directions. Mr. Andrew Carnegie has promised £1,000 a year for three years to endow entomological scholarships for three qualified medical men, who are to proceed to America and study entomology, in order to go later to Africa, where there is much work to be done by trained entomologists.

Besides the Royal Society's Sleeping Sickness Commission, to which I have referred, the British South Africa Company appointed a Commission in 1911—consisting of Dr. A. W. May, Principal Medical Officer of Northern Rhodesia; Dr. A. Kinghorn, of the Liverpool School of Tropical Medicine; and Dr. J. R. Leech, of the Rhodesian Medical Staff; besides a trained entomologist and a bacteriologist—to study the disease in Rhodesia.

Another expedition, including Dr. J. L. Todd and Dr.

S. B. Wolbach, was sent in 1911 by the Liverpool School of Tropical Medicine to the West African Colony of the Gambia to make further study concerning the value of gland puncture in diagnosing sleeping sickness. They quote a French trader who told them of one district where so many women, working in the rice fields and therefore much exposed to the tsetse fly, had died of sleeping sickness, that one man had lost five wives from that disease in two years.

The Belgian Commission, under Dr. Rodhain, has its headquarters at Katanga, in the south-east corner of the Belgian Congo, and has lately examined the route of the proposed railway from Kambove to Bukama. They find that *G. palpalis* only exists at two points on the route, where prophylactic measures must be taken. The number of Belgian lazarets, with one or two doctors in charge, is now 27, in 17 of which 2,224 sleeping sickness patients were treated last year. Attached to the lazarets are 31 sanitary brigades, consisting of 1,680 labourers, who are employed in clearing the neighbourhood of the lazarets, caravan roads, railway tracks, fords and landing places.

Entomologists are busy, too, for Mr. Carpenter, under the auspices of the Tropical Diseases Committee of the Royal Society, is studying the bionomics of *G. palpalis* in Uganda, while Miss Robertson is also there endeavouring to find out what happens to the trypanosomes during their mysterious life in the interior of the tsetse fly.

We cannot praise too highly those brave men and women who are toiling in a bad climate, with endless difficulties to overcome, in the endeavour to rid Africa of this curse, which threatens to ruin the brightest prospects of our great possessions in that continent. Death has claimed his victims among our countrymen, and others have had to fall out broken in health and spirits.

One exceptionally sad case was that of Lieutenant Forbes Tulloch, R.A.M.C., who, while a member of the Royal Society's Sleeping Sickness Commission in Uganda, had the misfortune to cut himself during the dissection of an infected rat. Trypanosomes soon appeared in his blood, and, after an unusually rapid course, the infection ended fatally in

London in June, 1906, after an illness of only a few months.

Well may the poet say of such as these :—

"Take up the white man's burden—
The savage wars of peace—
Fill full the mouth of famine
And bid the sickness cease ;
And when your goal is nearest,
The end for others sought,
Watch sloth and heathen folly
Bring all your hope to nought.

"Take up the white man's burden—
No tawdry rule of kings,
But toil of serf and sweeper—
The tale of common things.
The ports ye shall not enter,
The roads ye shall not tread,
Go make them with your living,
And mark them with your dead."

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